METHOD OF TRANSPORTING A CHIMERIC HYBRID MOLECULE ACROSS THE BLOOD BRAIN BARRIER

AMENDMENT NO 2 TO CLAIMS

(twice amended) 1. A method of transporting a pharmacologically active peptide across the blood brain barrier into the central nervous system of a living subject, by administration to said subject ~~of~~ a conjugate molecule comprising said peptide covalently linked to a non-peptide mu (μ) opioid receptor agonist, comprising:

a. Selecting ~~The selection of~~ a non-peptide mu (μ) opioid receptor agonist and a cross-linker, such that when the mu (μ) opioid receptor agonist is modified and covalently linked to the cross-linker and the cross-linker is covalently linked via a peptide bond to the pharmacologically active peptide, the cross-clinker will be able to flex such that the mu (μ) opioid opioid receptor agonist and the pharmacologically active peptide contemporaneously activate their respective receptors;

b. Modifying ~~The modification of~~ the mu (μ) opioid receptor agonist such that it can be covalently attached to a flexible cross-linker, the covalent attachment of the

modified mu (μ) opioid receptor agonist to the flexible hinge cross-linker, and the covalent attachment of the cross-linker via a peptide bond to the pharmacologically active peptide, to form a conjugate molecule; and

c. Administering ~~The administration of~~ a pharmaceutical composition of said conjugate molecule to said living subject.

(once amended) 2. The method of claim 1 wherein the mu opioid receptor agonist is a pharmacologically active opioid.

3. The method of claim 2 wherein the opioid is a pharmacologically active form of morphine.

4. The method of claim 1 wherein the peptide is a pharmacologically active form of Substance P.